



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference J 10018 PCT		FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA416)
International application No. PCT/EP 03/14844	International filing date (day/month/year) 23.12.2003	Priority date (day/month/year) 23.12.2002	
International Patent Classification (IPC) or both national classification and IPC C07C255/25			
Applicant JERINI AG et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"><input checked="" type="checkbox"/> Basis of the opinionII <input type="checkbox"/> PriorityIII <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicabilityIV <input type="checkbox"/> Lack of unity of inventionV <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statementVI <input type="checkbox"/> Certain documents citedVII <input type="checkbox"/> Certain defects in the international applicationVIII <input type="checkbox"/> Certain observations on the international application			
Date of submission of the demand 08.07.2004		Date of completion of this report 17.01.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer Romano-Götsch, R Telephone No. +49 89 2399-8874 	

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**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP 03/14844

I. Basis of the report

With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-130 as originally filed

Claims, Numbers

as originally filed

Drawings, Sheets

1/8-8/8 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-87 (part)

because:

☒ the said international application, or the said claims Nos. 85-86 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-87 (part)

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Yes: Claims

No: Claims 18

Inventive step (IS)

Yes: Claims

No: Claims 1-87

Industrial applicability (IA)

Yes: Claims

No: Claims 1-84, 87, (85-86 no opinion)

2. Citations and explanations

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see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Present claims 1-87 have not been searched completely (see Search Report). According to Rule 66.1(e) PCT, the subject-matter for which no international search report has been established need not be the subject of an international preliminary examination. Consequently, the opinion below is directed to the part of claims 1-87 which have been searched, corresponding to the compounds of pp. 82-122.

The Applicant's attention is also directed to the fact that claims 85 and 86 are directed to a method of treatment of the animal body, i.e. they contain subject-matter which no International Authority shall be required to examine (Rule 67.1(iv) PCT). Consequently, an opinion in respect to the industrial applicability of said claim is not established in the present written opinion.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following document is referred to in this communication:

D1: WO-A-00/27811

1. Novelty

The present application does not meet the requirements of Art. 33(2) PCT because the subject-matter of claims 18 is not novel.

Claim 18 is directed to "a compound". The fact that preferably that the compound is according to claims 1-17 with the structure formula (I) is not relevant, being this an optional feature.

D1 describes derivatives of pyridinemethyl diamide and carbamate and their activity as inhibitors of the rotamase FKBP12. Thus D1 anticipates the novelty of claim 18 as presently drafted. The compounds disclosed in D1 are structurally different from the ones of claims 1-17, 19-87 file.

2. Inventive step

The present application does not meet the requirements of Art. 33(3) PCT.

Art. 33(3) PCT requires the proposed solution for a given technical problem not to be obvious to a skilled person departing from the state of the art.

If the inventive step of a claimed invention is based on a given technical effect, the latter should, in principle, be achievable over the whole area claimed.

In view of D1, the technical problem which the present application addresses is the provision of further chemical compounds with inhibitory rotamase activity.

The proposed solution are the compounds of present claims 1-33 (especially claim 18 as

presently drafted).

To solve the technical problem, all the claimed compounds need to possess this inhibitory activity, being this technical effect the sole possible reason for the inventiveness of the compounds on file.

The examples on file (Table pp.126-129) provide evidence of inhibitory rotamase activity only for some of the compounds falling under the scope of present claims 1-87 and for some of the enzymes tested (namely T-1 and T-5).

It is well known that enzymes are extremely specific in the recognition of substrates, due to the strict steric requirements of the enzymes binding sites. Any even minimal structural modification can turn down the activity of a potent inhibitor or viceversa (compare for example the % inhibition of compounds 26 and 43 on Table 2 of D1 (p.62)). Furthermore, a potent inhibitor for one enzyme, could be a bad inhibitor for another enzyme.

Therefore, the evidence of the Table on p. 126 on file cannot be regarded as sufficient evidence to lead to the inference that substantially all the claimed compounds and "prodrug thereof" (whatever is meant by it) inhibit all rotamase enzymes, because it is not credible that substantially all compounds on file possess the claimed inhibitory activity. Therefore the requirements of Art.33(3) PCT are not met. This is even more true for those compounds that are undefined such as the "prodrugs" of the claimed compounds recited in the claims (see for examples claims 1,27,33,61,63, etc.).

3. Industrial Applicability

Turning to the question whether claims 85 and 86 are industrially applicable, no unified criteria exist in the PCT. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not regard as industrially applicable claims to the use of a compound in medical treatment, however will allow claims to a known compound for first use in medical treatment and the use of such compound for the manufacture of a medicament for a new medical treatment.

4. Lack of Support

Claims 38-62 are directed to the use of the compounds on file for the manufacture of a medicament for the treatment/prevention of a series of pathologies. While it is well known in the art that rotamases are involved in cell proliferation and neurodegenerative processes, there is no evidence on file to support that the presently claimed compounds are effective antiviral, antiparasite and antifungal agents, or are effective against gynecological and dermatological infections, stroke, inflammatory diseases, immune based disorders, heart diseases, cardiovascular or heart diseases (claims 40, 42-43). Nor there is evidence on file that the claimed compounds are effective against any of the specific disorders listed in claims 41, 44-62. As a matter of fact the application provides no data at all to support any therapeutical application.

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It follows that the subject-matter of claims 38-62 is speculative and thus fails to meet the requirements of Art. 6 PCT.